

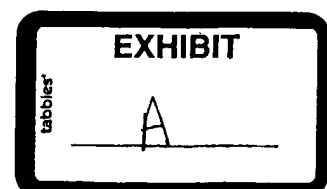
A circular black ink stamp from the Intellectual Property Office (IPO). The text "O I P E" is curved along the top inner edge, "J C I O" is curved along the top outer edge, "APR 26 2004" is in the center, and "PATENT & TRADEMARK OFFICE" is curved along the bottom inner edge.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

AFFIDAVIT OF EDWARD T. MICKELSON

COUNTY OF HARRIS

2. I am a registered patent agent employed by Winstead Sechrest & Minick P.C. and hold a doctorate in chemistry from Rice University (Houston, TX). I have reviewed the statements herein and believe, to the best of my abilities, that they are true and correct.



3. Pursuant to Applicant's April 9, 2004 interview with Examiner Choi and filed concurrently with Applicant's response to the Office Action mailed December 18, 2003, Applicant hereby provides the requested affidavit (as Exhibit A) detailing the levels of ascorbic acid in the compositions of Duffy et al. ("*Duffy*") (U.S. Patent 5,516,793).

4. Claims 1-3, 10, 15-18, 24, and 25 of the above-identified Application have been rejected under 35 U.S.C. § 102(b) as being unpatentable over Duffy et al. ("*Duffy*") (U.S. Patent 5,516,793).

5. The Examiner has stated that *Duffy* expressly discloses a composition comprising demineralized water, propylene glycol, glycerin, hydroxyethylcellulose, Tween 20, ammonium hydroxide, glycolic acid and ascorbic acid (5% or 10%), having a pH of 3.7 (5%) and 3.8 (10%). The Examiner has also stated that with respect to claim 24, the term "about 15%" is not defined, as such, the Examiner has read the term "about" to include 10%. See Office Action, page 2, fourth full paragraph.

6. All of the above-rejected claims require a composition comprising at least 5.0% (w/v) ascorbic acid in water, and a pH greater than 3.5. Such compositions, comprising relatively high pH values for such relatively high concentrations of ascorbic acid, are made possible by the stabilizing treatments described in Application. Without such treatments, the ascorbic acid rapidly degrades at pH values greater than 3.5 to yield solutions that comprise less than 5.0%(w/v) ascorbic acid. With regard to *Duffy*, Applicant respectfully points out that the Examiner is assuming that there is no reaction of components within the mixtures and that the resulting compositions of *Duffy* are simply the sum of the initial components. Reaction of the components of *Duffy* does occur, however, and the resulting compositions disclosed therein do not comprise at least 5.0% (w/v) ascorbic acid in the admixed formulation.

7. *Duffy* describes the addition of ascorbic acid to topical formulations for the purpose of reducing irritation caused by another active ingredient. Unlike in the compositions of the present invention, however, ascorbic acid is not the active ingredient in the compositions of *Duffy*. Referring to *Duffy*, col. 7, ll. 8-31 (Example II), Compositions E and F are formulated (in part) with 5 and 10wt.% ascorbic acid, and have resulting pH values of 3.7 and 3.8, respectfully. However, in each of these compositions, sufficient base (ammonium hydroxide) is added to convert all or most of the ascorbic acid present in the formulation to the unstable ascorbate anion (with is easily oxidized).

8. Composition E comprises the following:

2.700 wt% ammonium hydroxide (NH_4OH), M.W. = 35 g/mol

4.000 wt% glycolic acid (CH_2OHCOOH), M.W. = 76 g/mol

5.000 wt% ascorbic acid ($\text{C}_6\text{H}_8\text{O}_6$), M.W. = 176 g/mol

9. Assuming 100 grams total (total amount is really arbitrary, but this assumption simplifies the calculation. Note that *Duffy* never actually listed amounts).

10. Molar amounts are calculated as follows:

Ammonium hydroxide = $2.700 \text{ g} \div 35 \text{ g/mol} = 0.077 \text{ mol}$, normalized to 2.8

Glycolic acid = $4.000 \text{ g} \div 76 \text{ g/mol} = 0.053 \text{ mol}$, normalized to 1.9

Ascorbic acid = $5.000 \text{ g} \div 176 \text{ g/mol} = 0.028 \text{ mol}$, normalized to 1

11. Thus, there is roughly three times as much NH_4OH (on a mole basis) as ascorbic acid in *Duffy's* Composition E. Even if it is assumed that the NH_4OH preferentially "neutralizes" all of the glycolic acid present, there is still enough NH_4OH present to convert more than 85% of the ascorbic acid to the ascorbate anion, as shown in the calculation below:

$0.077 \text{ mol ammonium hydroxide} - 0.053 \text{ mol glycolic acid} = 0.024 \text{ mol ammonium hydroxide.}$

$0.028 \text{ mol ascorbic acid} - 0.024 \text{ mol ammonium hydroxide} = 0.004 \text{ mol ascorbic acid remaining.}$

$0.004 \text{ mol ascorbic acid} \times 176 \text{ g/mol} = 0.70 \text{ g ascorbic acid remaining, or about } 0.7 \text{ wt\% in the composition.}$

12. Composition F comprises the following:

4.300 wt% ammonium hydroxide (NH_4OH), M.W. = 35 g/mol

4.000 wt% glycolic acid (CH_2OHCOOH), M.W. = 76 g/mol

10.000 wt% ascorbic acid ($\text{C}_6\text{H}_8\text{O}_6$), M.W. = 176 g/mol

13. Assuming 100 grams total:

Molar amounts are calculated as follows:

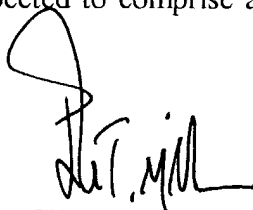
Ammonium hydroxide = $4.300 \text{ g} \div 35 \text{ g/mol} = 0.12 \text{ mol}$, normalized to 2.3

Glycolic acid = $4.000 \text{ g} \div 76 \text{ g/mol} = 0.053 \text{ mol}$, normalized to 1

Ascorbic acid = $10.000 \text{ g} \div 176 \text{ g/mol} = 0.057 \text{ mol}$, normalized to 1.1

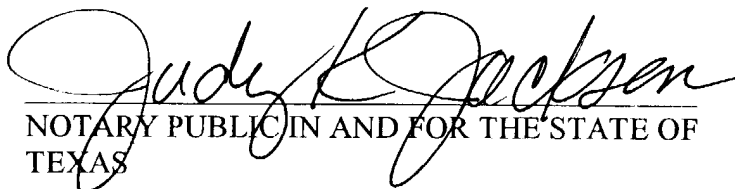
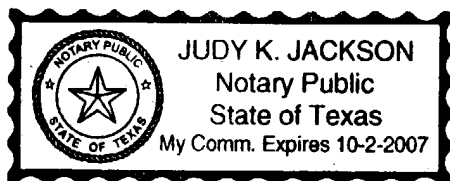
14. Thus, there is enough NH_4OH present to convert all of both the glycolic acid and ascorbic acid to their conjugate base forms (the ascorbate anion in the case of ascorbic acid). Thus, such compositions of *Duffy* cannot be expected to comprise any more than about 1wt.% ascorbic acid in their final admixed form.

FURTHER AFFIANT SAYETH NOT



Edward T. Mickelson

19th day April, 2004.



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